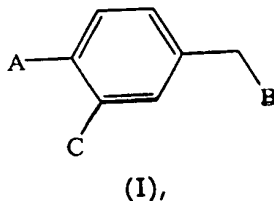


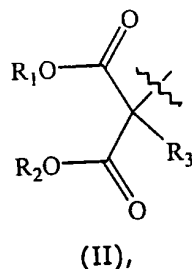
WHAT IS CLAIMED IS:

1. A compound of formula I:



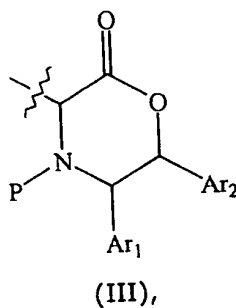
wherein:

A is carboxyl, carboxyalkyl, dicarboxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, dialkoxycarbonylalkyl, or a malonyl group of formula II:

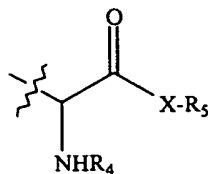


wherein R_1 and R_2 may be the same or different and are selected from the group consisting of hydrogen, alkyl, aryl, arylalkyl, alkylaryl, and heteroaryl; and R_3 is selected from the group consisting of hydrogen, halo, hydroxy, amino, alkyl, aryl, and alkoxy;

B has the formula III:



wherein P is an amine protective group; and Ar_1 and Ar_2 are aryl groups; or the formula IV:



(IV),

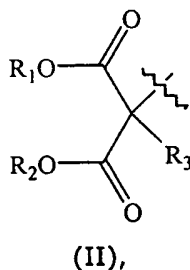
- wherein X is NH or O; R₄ is hydrogen, alkyl, aryl, alkylaryl, arylalkyl, or an amine protective group; and R₅ is selected from the group consisting of hydrogen, alkyl, aryl, arylalkyl, alkylaryl, and heteroaryl; and

C is selected from the group consisting of hydrogen, hydroxyl, alkyl, alkylcarbonyl, alkylcarbonyloxy, alkoxycarbonyl, and alkoxycarbonyl alkyl;

- wherein said aryl, heteroaryl, and the aryl portion of said arylalkyl and alkylaryl may be unsubstituted or substituted with a substituent selected from the group consisting of alkyl, hydroxy, halo, keto, amino, and alkoxy; with the provisos that (i) R₅ is not hydrogen when A is carboxyl or carboxyalkyl, C is hydrogen, B has the formula IV wherein R₄ is hydrogen or alkylcarbonyl, and X is NH; and (ii) R₅ is not hydrogen or alkyl when A is carboxyl or carboxyalkyl, C is hydrogen or hydroxy, B has the formula IV wherein R₄ is hydrogen or alkylcarbonyl, and X is O.

2. The compound of claim 1, wherein:

- A is carboxyl, carboxyl C₁-C₆ alkyl, dicarboxy C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, C₁-C₆ alkoxycarbonyl C₁-C₆ alkyl, C₁-C₆ dialkoxycarbonyl C₁-C₆ alkyl, or a malonyl group of formula II:



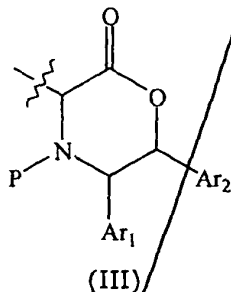
(II),

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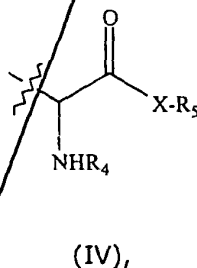
wherein R₁ and R₂ may be the same or different and are selected from the group consisting of hydrogen, C₁-C₆ alkyl, aryl, aryl C₁-C₆ alkyl, C₁-C₆

alkylaryl, and heteroaryl; and R_3 is selected from the group consisting of hydrogen, halo, hydroxy, amino, C_1 - C_6 alkyl, aryl, and C_1 - C_6 alkoxy;

B has the formula III:



wherein P is an amine protective group; and Ar_1 and Ar_2 are aryl groups; or B has the formula IV:



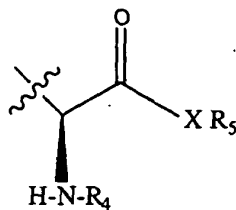
wherein X is NH or O; R_4 is hydrogen, C_1 - C_6 alkyl, aryl, C_1 - C_6 alkylaryl, aryl C_1 - C_6 alkyl, or an amine protective group; and R_5 is selected from the group consisting of hydrogen, C_1 - C_6 alkyl, aryl, aryl C_1 - C_6 alkyl, C_1 - C_6 alkylaryl, and heteroaryl; and

C is selected from the group consisting of hydrogen, hydroxyl, C_1 - C_6 alkyl, C_1 - C_6 alkylcarbonyl, C_1 - C_6 alkylcarbonyloxy, C_1 - C_6 alkoxy carbonyl, and C_1 - C_6 alkoxy carbonyl C_1 - C_6 alkyl; wherein said aryl, heteroaryl, and the aryl portion of said arylalkyl and alkylaryl may be unsubstituted or substituted with a substituent selected from the group consisting of C_1 - C_6 alkyl, hydroxy, halo, keto, amino, and C_1 - C_6 alkoxy.

3. The compound of claim 2, wherein B has the formula IV.

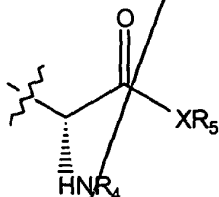
4. The compound of claim 3, wherein B has the formula:

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- wherein X is NH or O; R₄ is hydrogen, C₁-C₆ alkyl, aryl, C₁-C₆ alkylaryl, aryl C₁-C₆ alkyl, or an amine protective group; and R₅ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, aryl, aryl C₁-C₆ alkyl, C₁-C₆ alkylaryl, and heteroaryl.

5. The compound of claim 3, wherein B has the formula:



10

- wherein X is NH or O; R₄ is hydrogen, C₁-C₆ alkyl, aryl, C₁-C₆ alkylaryl, aryl C₁-C₆ alkyl, or an amine protective group; and R₅ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, aryl, aryl C₁-C₆ alkyl, C₁-C₆ alkylaryl, and heteroaryl.

15

6. The compound of claim 4 or 5, wherein X is O.

20 7. The compound of claim 6, wherein R₄ is hydrogen.

8. The compound of claim 6, wherein R₄ is an amine protecting group.

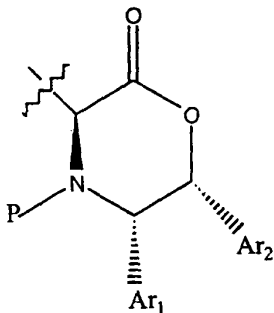
9. The compound of claim 8, wherein acid amine protecting group is selected from the group consisting of fluorenylmethoxycarbonyl, tert-butoxycarbonyl, carbobenzoxy, and carbamoyl.

25

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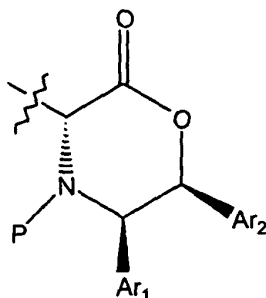
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10. The compound of claim 8, wherein R_5 is hydrogen.
11. The compound of any of claims 4-10, wherein R_1 and R_2 are hydrogen.
- 5 12. The compound of claim 11, wherein R_3 is hydrogen.
13. The compound of any of claims 4-12, wherein C is hydrogen.
14. The compound of any of claims 4-12, wherein C is C_1 - C_6 alkylcarbonyl.
- 10 15. The compound of any of claim 4-12 and 14, wherein C is tert-butoxycarbonyl.
16. The compound of any of claims 4-12, wherein C is C_1 - C_6 alkylcarbonyloxy.
- 15 17. The compound of any of claims 4-12 and 16, wherein C is acetyloxy.
18. The compound of claim 1 or 2, wherein B has the formula III.
- 20 19. The compound of claim 18, wherein B has the formula:



20. The compound of claim 18, wherein B has the formula:

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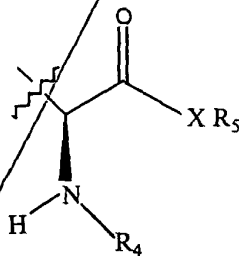


21. The compound of claim 19 or 20, wherein Ar₁ and Ar₂ are phenyl.

5 22. The compound of any of claims 18-21, wherein said amine protecting group is selected from the group consisting of fluorenylmethoxycarbonyl, tert-butoxy carbonyl, carbobenzoxy, and carbamoyl.

23. The compound of claim 9 or 22, wherein said amine protecting group is
10 fluorenylmethoxycarbonyl.

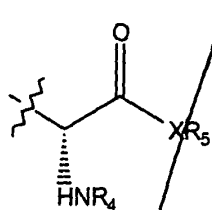
Sub 24. The compound of claim 1 or 2, wherein R₁ and R₂ are tert-butyl and R₃ is
As- hydrogen, and B has the formula



15

wherein X is O, R₄ is fluorenylmethoxycarbonyl, and R₅ is hydrogen.

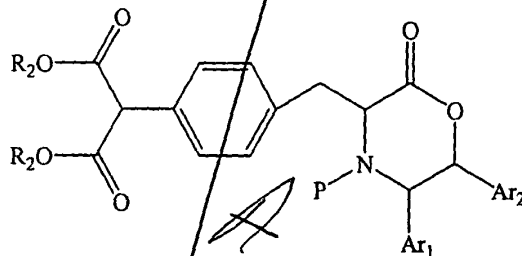
25. The compound of claim 1 or 2, wherein R₁ and R₂ are tert-butyl, and R₃ is
20 hydrogen; and B has the formula



wherein R_4 is fluorenylmethoxycarbonyl.

R-126

- 5 ²⁶ 25. A process for the preparation of a compound of formula VII:

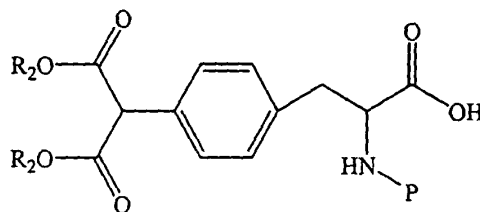


(VII),

wherein R_2 is alkyl, P is an amine protecting group, and Ar_1 and Ar_2 are aryl;

- 10 the process comprising:
- (a) converting a p-halotoluene to a p-tolyl-malonic acid dialkyl ester by contacting the p-halotoluene with a dialkylmalonate and a cuprous halide;
- (b) halogenating the p-tolyl-malonic acid dialkyl ester to obtain a (4-halomethylphenyl)-malonic acid dialkyl ester; and
- 15 (c) contacting the (4-halomethylphenyl)-malonic acid dialkyl ester with a benzyl-6-oxo-2,3-diaryl-4-morpholine to obtain the compound of formula VII.

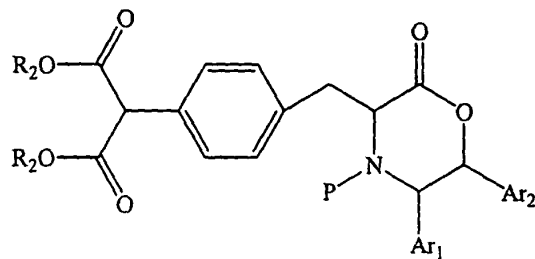
- ³² 26. A process for preparing a compound of formula VIII:



(VIII),

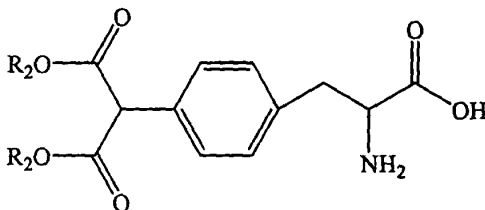
wherein R_2 is alkyl and P is an amine protecting group; the process comprising:

(a) reducing the compound of formula



(VII),

to obtain a compound of formula IX:

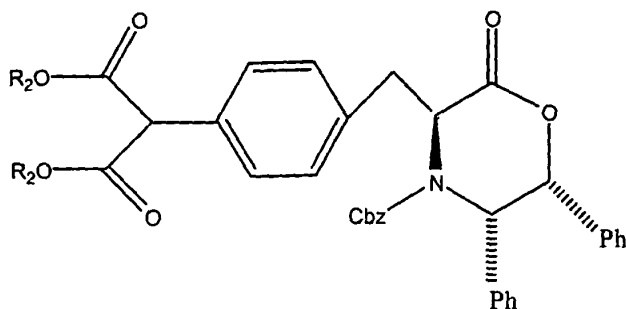


(IX);

and

(b) reacting the compound of formula IX with an amine protecting agent to obtain the compound of formula VIII.

¹⁸/₂₇. The process of claim ¹⁷/₂₆, wherein the compound of formula VII is:



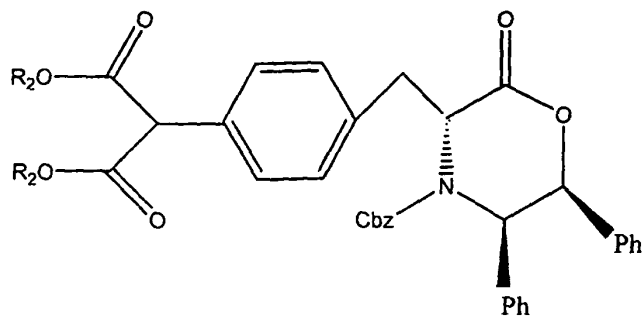
(VIIa)

wherein said benzyl-6-oxo-2,3-diphenyl-4-morpholine is benzyl (2R,3S)-(-)-6-oxo-2,3-diphenyl-4-morpholine.

5

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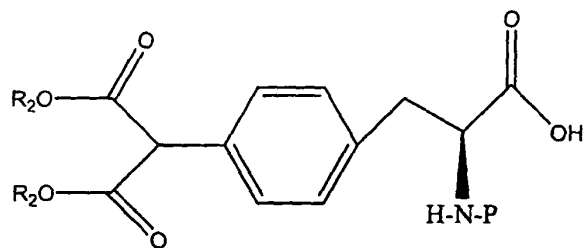
28. The process of claim 27, wherein the compound of formula VII is:



(VIIb)

30

10 29. A process for preparing a compound of formula VIIIa:



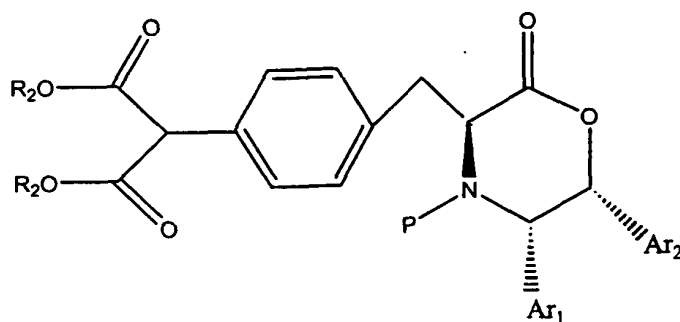
(VIIIa)

wherein R_2 is alkyl and P is an amine protecting group; the process comprising:

20

(a) reducing a compound of formula VII

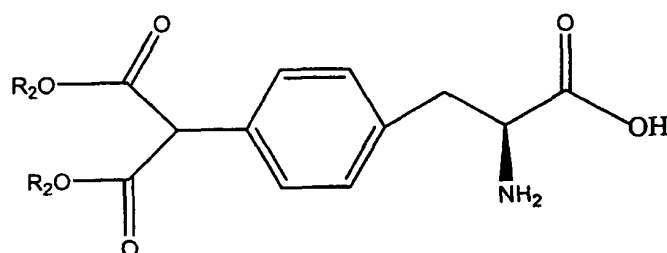
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(VIIa)

to obtain a compound of formula IXa:

5



(IXa);

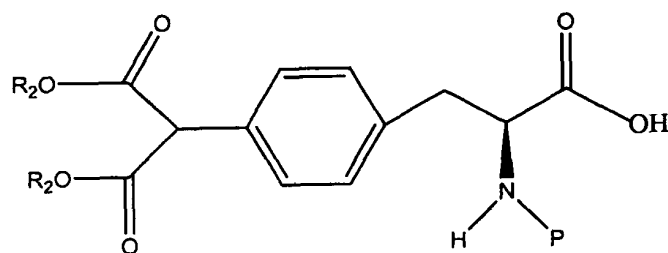
10 and

(b) reacting the compound of formula IXa with an amine protecting agent to obtain the compound of formula VIII.

3/

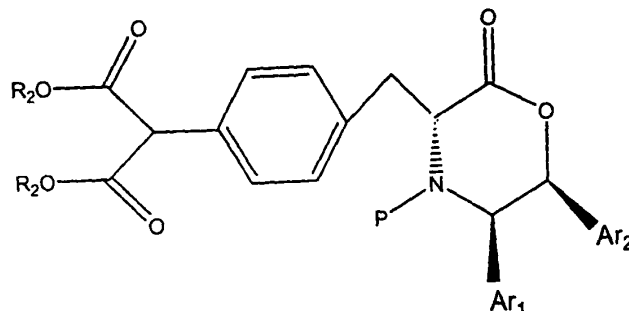
30. A process for preparing a compound of the formula:

15

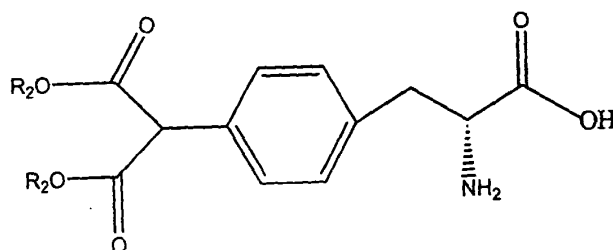


wherein R_2 is alkyl and P is an amine protecting group; the process comprising:

(a) reducing a compound of formula:



5 to obtain a compound of formula IXb:



(IXb);

and (b) reacting the compound of formula IXa with an amine protecting agent to obtain the compound of formula VIII.

³²
~~31~~. The process of claim ²⁸~~27~~, wherein said p-halotoluene is p-iodotoluene.

³³
~~32~~. The process of claim ²⁹~~27~~, wherein said (4-halomethylphenyl)-malonic acid dialkyl is (4-bromomethylphenyl)-malonic acid dialkyl ester.

15 ³⁴
~~33~~. The process of any of claims ~~27-32~~, wherein R₂ is t-butyl.

³⁵
~~34~~. A conjugate comprising a conjugant covalently linked to a compound of any of claims ~~1-25~~.

³⁶
~~35~~. The conjugate of claim ~~34~~, wherein said conjugant is an amino acid or a polypeptide.

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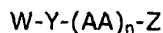
³⁶ 36. The conjugate of claim ~~34~~, wherein said conjugant is a nucleic acid or a nucleotide.

³⁸

5 ³⁷ 37. The conjugate of claim ~~34~~, wherein said conjugant is a polymer.

³⁹

³⁸ 38. A compound of the formula:



wherein n is 0 to 15;

- 10 Y is a phenylalanyl radical having a phenyl ring, an amine end, and a carboxyl end, the phenyl ring having one or more substituents selected from the group consisting of hydroxyl, carboxyl, formyl, carboxyalkyl, carboxyalkyloxy, dicarboxyalkyl, dicarboxyalkyloxy, dicarboxyhaloalkyl, dicarboxyhaloalkyloxy, and phosphonoalkyl, phosphonohaloalkyl, wherein the
- 15 alkyl portion of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, aminoalkyl, alkyl, alkoxy, and keto;

- W is a moiety attached to the nitrogen of Y and is selected from the group consisting of alkylcarbonyl, oxalyl, alkylaminooxalyl, arylaminooxalyl,
- 20 arylalkylaminooxalyl, alkoxyoxalyl, carboxyalkyl carbonyl, heterocyclyl carbonyl, heterocyclylalkyl carbonyl, arylalkyl heterocyclylalkyl carbonyl, aryloxy carbonyl, and arylalkoxy carbonyl, wherein the aryl and alkyl portions of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino,
- 25 aminoalkyl, alkyl, alkoxy, and keto; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S;

AA is an amino acid, the amine end of which is attached to the carboxyl end of Y; and

Z is an arylalkylamino or arylheterocyclyl alkylamino;

- 30 or a salt thereof;

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with the proviso that W is not arylalkylamino when the phenyl ring of phenylalanyl contains a phosphonoalkyl or phosphonohaloalkyl substituent at a position para to the alkylamido group and the ortho and meta positions are unsubstituted.

5 ~~40~~

~~39~~. The compound of claim ~~38~~, wherein n is 0 to 15;

Y is a phenylalanyl radical having a phenyl ring, an amine end, and a carboxyl end, the phenyl ring having one or more substituents selected from the group consisting of hydroxyl, carboxyl, formyl, carboxy C₁-C₆ alkyl,

- 10 carboxy C₁-C₆ alkyloxy, dicarboxy C₁-C₆ alkyl, dicarboxy C₁-C₆ alkyloxy, dicarboxyhalo C₁-C₆ alkyl, dicarboxyhalo C₁-C₆ alkyloxy, and phosphono C₁-C₆ alkyl, phosphonohalo C₁-C₆ alkyl, wherein the alkyl portion of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, aminoalkyl, C₁-C₆ alkyl,
- 15 C₁-C₆ alkoxy, and keto;

W is a moiety attached to the nitrogen of Y and is selected from the group consisting of C₁-C₆ alkylcarbonyl, oxalyl, C₁-C₆ alkylaminooxalyl, arylaminooxalyl, aryl C₁-C₆ alkylaminooxalyl, C₁-C₆ alkoxyoxalyl, carboxy C₁-C₆ alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C₁-C₆ alkyl carbonyl, aryl

20 C₁-C₆ alkyl heterocyclyl C₁-C₆ alkyl carbonyl, aryloxy carbonyl, and aryl C₁-C₆ alkoxy carbonyl, wherein the aryl and alkyl portions of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, amino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkoxy, and keto; and the heterocyclyl portion of W contains at least 4

- 25 hetero atoms selected from the group consisting of O, N, and S;

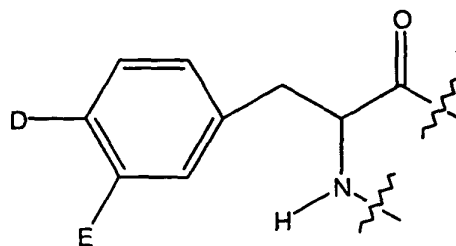
AA is an amino acid, the amine end of which is attached to the carboxyl end of Y; and

Z is an aryl C₁-C₆ alkylamino or arylheterocyclyl C₁-C₆ alkylamino; or a salt thereof.

30 ~~41~~

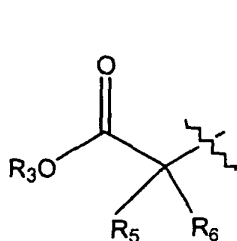
~~40~~. The compound of claim ~~39~~, wherein Y is of the formula XI:

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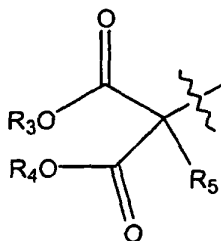


(XI)

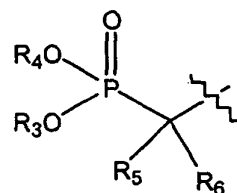
wherein D has the formula XII, XIII, or XIV:



(XII)



(XIII)



(XIV)

wherein R_3 and R_4 may be the same or different and are selected from the group consisting of hydrogen, C_1 - C_6 alkyl, aryl, aryl C_1 - C_6 alkyl, C_1 - C_6 alkaryl, and heteroaryl; and R_5 and R_6 may be the same or different and are selected from the group consisting of hydrogen, halo, hydroxy, amino, and C_1 - C_6 alkoxy; and

E is selected from the group consisting of hydrogen, C_1 - C_6 alkyl, C_1 - C_6 alkylcarbonyl, carboxyl, and C_1 - C_6 alkylcarbonyl C_1 - C_6 alkyl.

15

~~41~~⁴². The compound of claim ~~40~~, wherein D is of formula XII.

~~42~~⁴³. The compound of claim ~~40~~, wherein D is of formula XIII.

~~43~~⁴⁴. The compound of claim ~~40~~, wherein D is of formula XIV.

~~44~~⁴⁵. The compound of any of claims ~~41-43~~, wherein E is hydrogen.

~~45~~⁴⁶. The compound of claim ~~41~~, wherein E is carboxyl.

25

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⁴⁷
46. The compound of any of claim ~~41-45~~, wherein R₃, R₄, R₅, and R₆ are hydrogen.

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⁴⁸
47. The compound of claim ~~43~~, wherein R₃ and R₄ are hydrogen.

5

⁴⁹
48. The compound of any of claims ~~38-47~~, wherein W is selected from the group consisting of C₁-C₆ alkylcarbonyl, oxalyl, C₁-C₆ alkylaminooxalyl, arylaminooxalyl, aryl C₁-C₆ alkylaminooxalyl, C₁-C₆ alkoxyoxalyl, carboxy C₁-C₆ alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C₁-C₆ alkyl carbonyl, aryl C₁-C₆ alkyl heterocyclyl C₁-C₆ alkyl carbonyl, aryloxycarbonyl, and aryl C₁-C₆ alkoxycarbonyl, wherein the aryl and alkyl portions of the substituents may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, amino C₁-C₆ alkyl, C₁-C₆ alkyl, C₁-C₆ alkoxy, and keto; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S.

15

⁵⁰
49. The compound of any of claims ~~38-48~~, wherein W is C₁-C₆ alkyloxycarbonyl.

20

⁵¹
50. The compound of any of claims ~~38-49~~, wherein W is acetyl.

⁵²
51. The compound of any of claims ~~38-48~~, wherein W is oxalyl.

25

⁵³
52. The compound of any of claims ~~38-48~~, wherein W is carboxymethylcarbonyl.

⁵⁴
53. The compound of any of claims ~~38-48~~, wherein W is tetrazolylcarbonyl.

30

⁵⁵
54. The compound of any of claims ~~38-48~~, wherein W is tetrazolylmethylcarbonyl.

⁵⁶
55. The compound of any of claims ~~38-48~~, wherein W is an arylmethyloxycarbonyl.

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⁵⁷
~~56~~. The compound of any of claims 38-48 and 55, wherein W is an aminophenylmethyloxycarbonyl.

⁵⁸
~~57~~. The compound of any of claims 38-48 and 55-56, wherein W is 3-aminophenyl-1-methyloxycarbonyl.

⁵⁹
~~58~~. The compound of any of claims 38-48, wherein W is an aryloxycarbonyl.

⁶⁰
~~59~~. The compound of any of claims 38-48 and 58, wherein W is an naphthyloxycarbonyl.

⁶¹
~~60~~. The compound of any of claims 38-48 and 58-59, wherein W is an aminonaphthyloxycarbonyl.

⁶²
~~61~~. The compound of any of claims 38-48 and 58-60, wherein W is 6-amino-1-naphthyloxycarbonyl.

⁶³
~~62~~. The compound of any of claims 38-48, wherein W is an arylmethyltetrazolylmethylcarbonyl.

⁶⁴
~~63~~. The compound of any of claims 38-48 and 62, wherein W is a phenylmethyltetrazolylmethylcarbonyl.

⁶⁵
~~64~~. The compound of any of claims 38-48 and 62-63, wherein W is an alkoxyphenylmethyltetrazolylmethylcarbonyl.

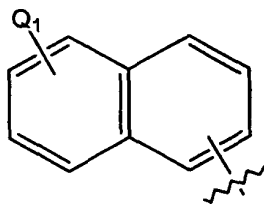
⁶⁶
~~65~~. The compound of any of claims 38-48 and 62-64, wherein W is a methoxyphenylmethyltetrazolylmethylcarbonyl.

⁶⁷
~~66~~. The compound of any of claims 38-65, wherein Z is aryl C₁-C₆ alkylamino.

⁶⁸
~~67~~. The compound of claim 66, wherein the aryl portion of Z has the formula:

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wherein Q_1 is hydrogen or a substituent selected from the group consisting of hydroxyl, halo, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, amino, and C_1 - C_6 acylamino.

5

~~68~~⁶⁹. The compound of claim 67, wherein the aryl portion of Z is attached to the alkylamino portion of Z at the aryl 1- or 2- position.

~~69~~⁷⁰. The compound of claim 67 or 68, wherein Q_1 is methyl.

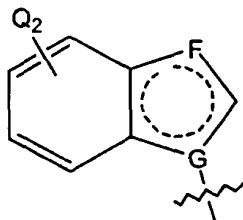
10

~~70~~⁷¹. The compound of any of claims 67-69, wherein Z is naphthylpropylamino.

~~71~~⁷². The compound of any of claims 38-65, wherein Z is aryl heterocyclyl C_1 - C_6 alkylamino.

15

~~72~~⁷³. The compound of claim 71, wherein the heterocyclyl portion of Z has the formula:



20

wherein Q_2 is hydrogen or a substituent selected from the group consisting of hydroxyl, halo, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, amino, and C_1 - C_6 acylamino, and F and G are independently selected from the group consisting of C, N, O, and S.

25

~~73~~⁷⁴. The compound of claim 72, wherein F is C and G is N.

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74. The compound of claim 72 or 73, wherein Q₂ is methyl.

76

75. The compound of any of claims 38-39, wherein W is selected from the group consisting of acetyl, oxalyl, C₁-C₆ alkylaminooxalyl, arylaminooxalyl, aryl C₁-C₆ alkylaminooxalyl, C₁-C₆ alkoxyoxalyl, carboxymethylcarbonyl, tetrazolylcarbonyl, tetrazolylmethylcarbonyl, aminophenylmethoxycarbonyl, amino naphthylloxycarbonyl, and methoxyphenylmethyl tetrazolylmethylcarbonyl.

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76. The compound of any of claims 38-75, wherein n is 1-3.

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77. The compound of any of claims 38-76, wherein said amino acid is selected from the group consisting of glycine, alanine, valine, norvaline, leucine, iso-leucine, norleucine, α -amino n-decanoic acid, serine, homoserine, threonine, methionine, cysteine, S-acetylaminomethyl-cysteine, proline, trans-3- and trans-4-hydroxyproline, phenylalanine, tyrosine, 4-aminophenylalanine, 4-nitrophenylalanine, 4-chlorophenylalanine, 4-carboxyphenylalanine, β -phenylserine β -hydroxyphenylalanine, phenylglycine, α -naphthylalanine, cyclohexylalanine, cyclohexylglycine, tryptophan, indoline-2-carboxylic acid, 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, aspartic acid, asparagine, aminomalonic acid, aminomalonic acid monoamide, glutamic acid, glutamine, histidine, arginine, lysine, N'-benzyl-N'-methyl-lysine, N',N'-dibenzyl-lysine, 6-hydroxylysine, ornithine, α -aminocyclopentane carboxylic acid, α -aminocyclohexane carboxylic acid, α -aminocycloheptane carboxylic acid, α -(2-amino-2-norbornane)-carboxylic acid, α,γ -diaminobutyric acid and α,β -diaminopropionic acid, homophenylalanine, and α -tert-butylglycine.

79

78. The compound of claim 77, wherein said amino acid is selected from the group consisting of glycine, alanine, leucine, iso-leucine, norleucine, cyclohexylalanine, 4-aminocyclohexylglycine, 4-acetylaminocyclohexylglycine, aspartic acid, asparagine, glutamic acid, and glutamine.

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79. The compound of any of claims 76-78, wherein n is 2.

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~~80~~⁸¹. The compound of claim 79, comprising a first amino acid (AA₁) attached to the phenyl alanine moiety and asparagine attached to said AA₁, wherein said AA₁ is selected from the group consisting of cyclohexylglycine, 4-aminocyclohexylglycine, and 4-acetylamino-cyclohexylglycine.

5

~~81~~⁸². The compound of claim 80, wherein said AA₁ is cyclohexylglycine.

~~82~~⁸³. The compound of claim 81, wherein D is of formula XIII, E, R₃, R₄, and R₅ are hydrogen, R₁ is oxalyl, and Z is naphthylpropylamino.

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~~83~~⁸⁴. The compound of claim 38 or 39, wherein Z is not indolylpropylamino when W is acetyl, and Y is a phenylalanyl radical having a phosphonomethyl substituent.

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~~84~~⁸⁵. A composition comprising a pharmacologically acceptable carrier and a compound of any of claims 38-83.

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~~85~~⁸⁶. A method for inhibiting an SH2 domain from binding with a phosphoprotein comprising contacting an SH2 domain with a compound of any of claims 34-83.

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~~86~~⁸⁷. The method of claim 85, wherein said SH2 domain is in a mammal, and said compound is administered to said mammal.

~~87~~⁸⁸. The use of a compound of any of claims 34-83 in the manufacture of a medicament for the treatment of a condition that responds to the inhibition of phosphoprotein binding to an SH2 domain of a mammal.

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~~88~~⁸⁹. The use of a compound of any of claims 34-83 in medicine.

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~~89~~⁹⁰. A compound of any of claims 34-83 for use as a Grb2-SH2 domain inhibitor.

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⁹¹
90. A method for inhibiting SH2 domain binding comprising exposing a material containing an SH2 domain to a compound of any of claims 34-83.

- ⁹²
91. A method for determining the presence of an SH2 domain in a material
- 5 comprising:
- (a) exposing a sample of said material to a SH2 binding compound and obtaining a first binding result;
- (b) exposing another sample of said material to a compound of any of claims 34-83 and obtaining a second binding result; and
- 10 (c) comparing the first and second binding results to determine whether an SH2 domain is present in the material.

- ⁹³
92. A method of preventing or treating a disease, state, or condition in a mammal comprising administering a compound of any of claims 34-83.
- 15 ⁹⁴
93. The method of claim 92, wherein the disease, state, or condition involves an SH2 domain binding.

- ⁹⁵
94. The method of any of claims 86, 92 or 93, wherein the mammal is
- 20 afflicted with a cancer.

- ⁹⁶
95. The method of claim 94, wherein the cancer is a breast cancer or ovarian cancer.

- ⁹⁷
96. The method of claim 86, 92, or 93, wherein the mammal is afflicted with a tumor.

- ⁹⁸
97. The method of claim 96, wherein the tumor is leukemia or lymphoma.

- ⁹⁹
98. The method of claim 96, wherein the tumor is a solid tumor.

- ¹⁰⁰
99. The method of claim 98, wherein the solid tumor is a brain tumor or a prostate tumor.

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- 101*
~~100~~. The method of claim 86, 92 or 93, wherein the mammal is afflicted with an autoimmune disease.
- 102*
~~101~~. The method of claim 86, 92, or 93, wherein the mammal is afflicted with an inflammatory disease.
- 103*
~~102~~. The method of claim 86, 92, or 93, wherein the mammal is afflicted with diabetes.
- 104*
~~103~~. The method of claim 86, 92, or 93, wherein the mammal is afflicted with obesity.
- 105*
~~104~~. The method of claim 86, 92, 93, wherein the mammal is afflicted with a metabolic disease.
- 106*
~~105~~. The method of claim 86, 92, or 93, wherein the mammal is afflicted with a cardiovascular disease.
- 107*
~~106~~. A method of enhancing the therapeutic effect of a treatment rendered to a mammal that has been afflicted with a disease, state, or condition, comprising administering to the mammal a compound of any of claims 34-83 in conjunction with the treatment.
- 108*
~~107~~. The method of claim 106, wherein the treatment comprises chemotherapy, radiation therapy, or biological therapy.
- 109*
~~108~~. The method of claim 107, wherein the biological therapy comprises the use of a protein.
- 110*
~~109~~. The method of claim 106 or 107, wherein the biological therapy comprises the use of an antibody or a recombinant protein.
- 111*
~~110~~. The method of any of claims 106-109, which comprises inhibiting a cell survival factor in the mammal.

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112

~~111~~. The method of any of claims 106-109, which comprises triggering cell apoptosis.

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113

~~112~~. A method of inhibiting the MAP kinase activity in a mammal comprising administering to the mammal a compound of any of claims 34-83.

114

~~113~~. The method of claim 94, wherein the cancer is mediated through BCR-Abl.

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~~114~~. The method of claim ~~92~~ or ~~93~~, which involves inhibiting the expression of erbB-2 receptor.

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